Docket N .: PF-0195-1 DIV

REMARKS

Applicants respectfully bring to the Examiner's attention an error in the communication of the Office Action of July 17, 2002 in which claims 11-16 and 21-24 are listed as pending. Claims 11-16 and 21-24 were canceled by Applicants in their Response to Office Action submitted April 26, 2002.

Amendments

Claim 25 has been canceled without prejudice or disclaimer and not for reasons related to patentablility. Claim 26, which depended from canceled claim 25, has been amended to depend from claim 1. Claim 1 has been amended to include the identification of a functional limitation of SEQ ID NO:, to expedite prosecution and not for reasons related to patentability, Applicants have amended Claim 1 b) to read, "a polypeptide comprising a naturally-occurring amino acid sequence at least 90% identical to the sequence of SEQ ID NO:1 over the entire length of SEQ ID NO:1, said polypeptide having serine protease activity." Support for this amendment may be found throughout the specification, for example, page 1, lines 16-23 in which amino acid residues H_{65}, D_{120}, and S_{213} in PSA, a serine protease of the kallikrein family were identified as being essential for serine protease activity, and page 11, lines 10-12 in which the same conserved residues critical for serine protease activity, H_{65}, D_{113}, and S_{206}, are identified in SEQ ID NO:1 (HPAK). Applicants respectfully request entry of the amendment to expedite prosecution or to further simplify matters for appeal.

Applicants have shown in the Response filed October 17, 2002 that HPAK shares homology with the kallikrein polypeptide family, a family consisting of members known to have undisputed utility, and therefore, homology can be used to show a substantial likelihood that the claimed polypeptide is similarly useful. Applicants need not show any more to demonstrate utility. Specifically, the kallikrein family includes kallikrein 11 which shares 90% sequence identity with HPAK. More specifically, as shown in Exhibits A and B (submitted in the October 17, 2002 response), SEQ ID NO:1 and kallikrein 11 are **100% identical** from residues L61-N253 of SEQ ID NO:1. Additionally, Kallikrein 11 has serine protease activity, is a useful marker for distinguishing prostate cancer and benign prostatic hypertrophy and is a potential new biomarker for prostate and ovarian cancer (LocusLink ID 11012; www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=11012, Exhibit L, enclosed herewith).

Therefore, Applicants' assertion that SEQ ID NO:1 also has serine protease activity would be found by one skilled in the art to be be more likely than not true.

Based on the high level of sequence homology, structural characteristics and tissue expression, Applicants have demonstrated a *prima facie* case for homology as an acceptable assertion of utility of the claimed polypeptides. Such an assertion of utility would be determined to be sound, scientific reasoning by one skilled in the art. Therefore, the Examiner must accept the Applicants' demonstration by homology that the claimed polypeptide is a member of the kallikrein polypeptide family and that the homology between the claimed invention and kallikrein polypeptides demonstrates utility by a reasonable probability, unless the Examiner can demonstrate through evidence or sound scientific reasoning that a person of ordinary skill in the art would doubt utility. The Examiner has failed to make such a showing. Thus, Applicants believe withdrawal of all outstanding rejections for reasons presented *supra* and in the Response to Office Action submitted October 17, 2002, is believed to be in order.

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CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding **objections/rejections.** Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Appellants invite the Examiner to contact Appellants' Attorney at

(650) 621-8555.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108**, as set forth in the enclosed fee transmittal letter.

Respectfully submitted,

INCYTE GENOMICS, INC.

Date: 17, December 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claim 25 has been canceled.

Claims 1 and 26 have been amended as follows:

1. **(Five Times Amended)** An isolated polypeptide selected from the group consisting of:

a) a polypeptide comprising the amino acid sequence of SEQ ID NO:1, and

b) a polypeptide comprising a naturally-occurring amino acid sequence at least 90% identical to the sequence of SEQ ID NO:1 over the entire length of SEQ ID NO:1, said polypeptide having serine protease activity.

26. **(Once Amended)** A composition comprising a polypeptide of claim [25] 1 and a suitable pharmaceutical carrier.

EXHIBIT L

Docket No.: PP-0195-1 DIV
USSN:09/170,980
Exhibit No. L

NCBI LocusLink

PubMed Entrez BLAST OMIM Taxonomy Structure

LocusLink Home

KLK11 Index: Top of Page

Nomenclature

Overview

Function

Relationships

Map

RefSeq

GenBank

Links

LocusLink:

Collaborators

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FAQ

Help

Statistics

RefSeq:

Click to Display mRNA-Genomic Alignments (spanning 5801 bps)

PUB | OMIM | ACEVIEW | UNIGENE | MAP | VAR | GDB | e! | UCSC | MGC

KLK11: kallikrein 11

LocusID: 11012

RefSeq Summary: Kallikreins are a subgroup of serine proteases having diverse physiological functions. Growing evidence suggests that many kallikreins are implicated in carcinogenesis and some have potential as novel cancer and other disease biomarkers. This gene is one of the fifteen kallikrein subfamily members located in a cluster on chromosome 19. Alternate splicing of this gene results in two transcript variants encoding two different isoforms which are differentially expressed.

Proteome Summary: Trypsin-like serine protease; has serine protease activity

Locus Type: gene with protein product, function known or inferred

Product: kallikrein 11 isoform 1 preproprotein
kallikrein 11 isoform 2 precursor

Alternate Symbols: TLSP, PRSS20, MGC33060

Alias: hippostasin
protease, serine, trypsin-like
protease, serine, 20 trypsin-like

GeneRIF: Gene References into Function:

11782391 • Human kallikrein 11: a new biomarker of prostate and ovarian carcinoma.

11550212 • may be usefu marker for distinguishing prostate cancer and benign prostatis hypertrophy

• may be useful marker for distinguishing prostate cancer and benign prostatic hypertrophy

Gene Ontology™:

Term	Evidence	Source	Pub
serine-type peptidase	P	Proteome	pm

Other Ontologies:

Term	Evidence	Source	Pub
Hydrolase	NR	Proteome	pm
Protease (other than proteasomal)	NR	Proteome	pm

Mouse Homology Maps:

NCBI vs. MGD	7 cM	Prss20-pending	Hs Mm
UCSC vs. MGD	7 cM	Prss20-pending	Hs Mm

Chromosome:	19			mv
Cytogenetic:	19q13.3-q13.4		RefSeq	
Markers:	Chr. 19	SHGC-57422		mv
	Chr. 19	RH102947		mv

Category: REVIEWED

1. mRNA: NM_006853

Protein: NP_006844 kallikrein 11 isoform 1 preproprotein — **BL**

Transcript Variant: This variant (1) uses an alternate in-frame exon in the 5' UTR and 5' coding region, compared to variant 2. The encoded isoform (1) is shorter than isoform 2, has a distinct N-terminus, and is preferentially expressed in brain.

GenBank Source: BC022068

2. mRNA: NM_144947

Protein: NP_659196 kallikrein 11 isoform 2 precursor — **BL**

Transcript Variant: This variant (2) encodes the longer isoform (2) which is preferentially expressed in prostate.

GenBank Source: AB041036,BC022068

Category: NCBI Genome Annotation

Genomic Contig: NT_011109 **gb sv mv ev mm**

Haplotype reference

Annotation for this locus:

Evidence: supported by alignment with mRNA

mRNA: NM_144947

Protein: NP_659196 **BL**

Nucleotide	Type	Protein	
AC011473	g	AAG23257	BL
AF164623	g	AAD47815	BL
AF243527	g	AAG33364	BL
AB012917	m	BAA33404	BL
AB013730	m	BAA88713	BL
AB041036	m	BAA96797	BL
BC015551	m		
BC022068	m	AAH22068	BL

- **OMIM:** 604434
- **UniGene:** Hs.57771

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